Participant Information Sheet

Version 2.0, 09/02/2022

Title of Project: 'Oral microbiome - dietary nitrate' interactions and cognitive health in older age

Researcher name: Joanna L'Heureux

Invitation and brief summary:

Thank you for showing an interest in this study. Please read this information sheet carefully before deciding whether you would like to take part. If you at any time want to withdraw from the study you can do so without any negative consequences. There will be no disadvantages to you of any kind if you do not choose to participate. This project is funded by a philanthropic donation by Tom Morgan to the University of Exeter.

Purpose of the research:

Nitric oxide is an important molecule that is involved in many physiological processes such as maintaining blood pressure and cognitive function. Whilst nitric oxide is generated in the body, nitrate which is found in vegetables can also contribute to the amount of nitric oxide in the human body. Bacteria in the mouth are important for breaking down the nitrate that we get from food sources. As we age, our ability to produce nitric oxide may decline which could affect physiological and cognitive processes. Therefore, the types of bacteria in the mouth which cause dietary nitrate to break down to nitric oxide may be particularly important for cognitive function in older adults. In the present study, we aim to determine whether we can use dietary nitrate supplementation, using natural beetroot juice, to gain beneficial changes in the oral bacteria. We also want to find out whether such changes in the microbiome are related to any changes in cognitive function.

Why have I been approached?

We are looking for healthy male and female volunteers over 50 years of age. This study will recruit 60 people who have genes that may reflect a high risk of dementia, a medium risk of dementia and a low risk of dementia. These genes account for only small differences in risk and research has not confirmed whether they have any meaningful impact on the likelihood of a person developing dementia.

We are also recruiting people based on their performance in the PROTECT cognitive tests. Some participants will have shown low levels of cognitive change over the past three years, while others will not. We are looking at very small changes which would not be picked up in a clinic and they do not require any follow-up with a doctor.

None of the genetic or cognitive profiles used to identify you for this study are 'clinically relevant'. They are for research purposes only. For this reason, we are not able to disclose individual profiles to you as a participant.

You will have the opportunity to ask questions and clarify any issues you may be unsure of before deciding whether you want to take part.

Unfortunately, you will not be eligible to take part in the study if:

- You are a current smoker or have regularly smoked within the past year.
- You regularly drink alcoholic drinks that are >14% ABV (undiluted)
- You have used mouthwash and/or a tongue scraper within the past week.
- You have taken antibiotics within the past 3 months.
- You have a diagnosis of dementia.
- You have periodontitis, gingivitis or other oral disease.
- Your genome has not been assessed by PROTECT team for the database.

What would taking part involve?

Should you agree to participate in this study we will ask you to complete a 3-month diet recall and a physical activity questionnaire. We will also send you a mouth rinse sampling kit through the post. The mouth rinse sampling kit will contain a 50 mL tube which contains 10 mL of commercially available mouth rinse (Crest Scope Classic Mouthwash). You will be asked to vigorously swish the mouth rinse for 30 seconds in your mouth. Do not swallow the mouth rinse. You will then carefully spit the mouth rinse back into the 50 mL tube. We will then ask you to post the sample back to the laboratory using the prepaid postal box that you can drop off at any Royal Mail post box.

You will be asked to provide 2 mouth rinse samples during the study. The first sample will be at the start of the study. You will be asked to take this sample within 2-4 hours of your morning meal. The second mouth rinse sample will be after 12 weeks of drinking one 70-ml 'shot' of beetroot juice every day (BeetIt 'shot' manufactured by James White Drinks Ltd., Ipswich, UK). On the final day of 12 weeks' supplementation, we ask you to have your beetroot juice in the morning with your morning meal. You should take your second mouth rinse sample within 2-4 hours of your morning meal and your last beetroot juice drink. At the end of each week during the 12-week period we will ask you to complete a log of your juice intake by ticking am or pm for each day of the week. We will also ask you to complete the PROTECT online cognitive assessment before and after the 12-week supplementation period. During the study we will send you instructions and reminders of study tasks via email and text message. You will be randomly allocated to receive either a nitrate-rich beetroot juice or a low-nitrate beetroot juice placebo. We will only be able to tell you which supplement you received once you have completed the study.

What are the possible benefits of taking part?

You will receive a free supply of beetroot juice for 12 weeks. Both types of juice are 100% natural products, made of beetroot with a small amount lemon juice mixed in for flavour, and contain antioxidants such as vitamins and polyphenols. We believe that the results of this research will help scientists design dietary products and dietary guidance that could help slow down cognitive decline in older age.

What are the possible disadvantages and risks of taking part?

Swallowing small amounts of the mouth rinse may cause you to feel queasy or may cause diarrhea. These symptoms should quickly pass, but if they do not please see a healthcare professional. Daily ingestion of beetroot juice may result in beet-coloured urine and stools. These side effects are harmless and will disappear once you stop consuming beetroot products.

What Covid-19 Secure measures are in place?

This research does not involve any laboratory visits. You will be able to complete the study protocol from home with internet access, and you can post your samples back to us by dropping the sample kit in a Royal Mail post box.

To minimise risk of infection to everyone involved in this project, we have taken measures based on the current UK government guidance (https://www.gov.uk/guidance/working-safely-during-coronavirus-covid-19). The postal mouth rinse sampling kits are prepared in our research laboratory in compliance with Covid-19 regulations, and or research staff involved in preparing the postal sampling kits undergo regular twice-weekly Covid-19 lateral flow antigen (LFD) tests. The risk of Covid-19 transmission is therefore considered low.

What will happen if I don't want to carry on with the study?

You are able to stop taking part in this study at any time without reason and without any negative consequences.

How will my information be kept confidential?

The University of Exeter processes personal data for the purposes of carrying out research in the public interest. The University will endeavour to be transparent about its processing of your personal data and this information sheet should provide a clear explanation of this. If you do have any queries about the University's processing of your personal data that cannot be resolved by the research team, further information may be obtained from the University's Data Protection Officer by emailing informationgovernance@exeter.ac.uk, or at http://www.exeter.ac.uk/ig/

The University of Exeter will keep identifiable information about you for ten years after the study has finished. Anonymized information, such as your cognitive assessment and saliva sample data may be kept indefinitely and up until the study objectives have been achieved.

Your rights to access, change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the study, we will keep the information about you that we have already obtained. To safeguard your rights, we will use the minimum personally-identifiable information possible.

The University of Exeter will use your name and contact details to contact you about the research study, and make sure that relevant information about the study is recorded for your care, and to oversee the quality of the study. Individuals from the University of Exeter and regulatory organizations may look at your research records to check the accuracy of the research study. The only people in the University of Exeter who will have access to information that identifies you will be people who need to contact you to discuss issues directly relating to the study or audit the data collection process (PROTECT Study Team). The people who analyze the information will not be able to identify you and will not be able to find out your name or contact details. We will keep identifiable information about you from this study for 10 years after the study has finished.

When you agree to take part in a research study, the information about your health and care may be provided to researchers running other research studies in this organization and in other organizations. These organizations may be universities, NHS organizations or companies involved in health and care research in this country or abroad. This information will not identify you and will not be combined with other information in a way that could identify you. The information will only be used for the purpose of health and care research, and cannot be used to contact you or to affect your care. It will not be used to make decisions about future services available to you, such as insurance.

Will I receive any payment for taking part?

No. There will be no payment in return for taking part in this project.

What will happen to the samples I give?

Mouth rinse samples will be stored in a secure storage area while they are waiting for analysis. It is possible that these samples may be shipped to other secured facilities for analysis. It is also possible that there may be some left over sample after we have completed analysis for this project. You will have the opportunity on the consent form for this study to specify whether we may keep these samples to use for other studies. If you agree to this you may, if you wish, say whether there are some types of research that you do not want your samples used for. Any other study wishing to use your surplus samples must first obtain approval from our ethics committee.

What will happen to the results of this study?

The results from this study may be published in academic publications and conferences. We are not able to disclose individual profiles to you as a participant.

Who is organising and funding this study?

The sponsor for this study is the University of Exeter.

Who has reviewed this study?

This project has been reviewed by the Sport and Health Sciences Research Ethics Committee at the University of Exeter.

Further information and contact details

If you have any questions about our project, either now or in the future, please feel free to contact myself personally:

Miss Joanna L'Heureux
Email: j.lheureux3@exeter.ac.uk

If you are not happy with any aspect of the study and wish to make a complaint please contact: Gail Seymour, Research Ethics and Governance Manager, g.m.seymour@exeter.ac.uk, 01392 726621.

Thank you for your interest in this project.

Consent to Take Part

- I confirm that I have read the information sheet dated 09/02/2022 (version no 2) for the above project, which includes information on how it will be conducted in a Covid-19 secure environment. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.
- I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason and without my legal rights being affected.
- I understand that relevant sections of the data collected during the study may be looked at by members of the research team and individuals from the University of Exeter, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records.
- I understand that my genetic and cognitive status cannot be disclosed.
- I understand taking part involves providing 2 mouth rinse saliva samples and mailing the collected sample to the laboratory through the post.
- I understand taking part involves completing online questionnaires and cognitive assessments on 2 occasions.
- I understand taking part involves adhering to ingesting 70 ml of beetroot juice every day for 12 weeks.
- I understand taking part involves not being told whether I received nitrate-rich beetroot juice or a low-nitrate placebo until upon the completion of the study.
- I understand that my mouth rinse saliva samples may be transported to other laboratories within the UK or overseas for further analyses.
- I understand that any information given by me may be used in future reports, articles or presentations by the researchers.
- I understand that my data will be used for the purposes of: Shared with other researchers for use in future research studies, published in academic journals, used for teaching or training materials and/or in public engagement activities in the UK and overseas.
- I agree to take part in the above study.